Elanco US Inc.
2500 Innovation Way
Greenfield, IN 46140 USA

1-877-352-6261

By Electronic Mail

July 25, 2022

The Honorable Michael S. Regan
Administrator
Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

The Honorable Robert M. Califf
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Chairman Krishnamoorthi's July 18, 2022 letter regarding Seresto flea and tick collars

Dear Administrator Regan and Commissioner Califf:

I am writing on behalf of Elanco Animal Health Inc. ("Elanco") in response to the letter dated July 18, 2022 from House Oversight and Reform Committee, Subcommittee on Economic and Consumer Policy Chairman Raja Krishnamoorthi ("the Letter"). The Letter makes a number of claims regarding the safety of Seresto that are inconsistent with science-based evaluation. Elanco continues to stand behind Seresto's strong safety profile, and the Letter does not present any reliable, scientific information calling that safety profile into question.

Seresto's safety profile is well established: more than 80 regulatory bodies around the world have approved its use to protect pets from disease-carrying fleas and ticks. Indeed, after the recent congressional hearing, veterinarians have reaffirmed the safety of Seresto. For example, one article noted that "[d]irectors of two national animal poison centers — Pet Poison Helpline and the ASPCA Animal Poison Control Center — have reported no deaths associated with the collars," and quoted a board-certified veterinary toxicologist who explained that "[i]f you poll toxicologists and the veterinarians who recommend millions of these collars ... it's a nonissue."[1]

Seresto's safety profile is supported by extensive pre-market studies. As EPA is aware, Seresto underwent a robust pre-market review and registration process. Numerous studies, including toxicity studies, pharmacokinetic studies, safety studies, laboratory efficacy studies, and field efficacy studies, support the product's strong safety profile.

Elanco is aware of no sound, scientifically supportable studies that have cast any doubt on the safety profile of Seresto, and the Letter does not cite a single one. Instead, recent concerns relating to Seresto have been based on incident reports that Elanco has received, all of which it has reported to EPA, as required by law. EPA's guidance directs companies to report all adverse events to EPA, regardless of whether there is any evidence that the product, in this case Seresto, *caused* the adverse event. Importantly, EPA has explained that looking at aggregate incident numbers alone is not a valid methodology. Instead, the total number of products sold must also be considered—unsurprisingly,

[1] Lisa Wogan, "Veterinarians puzzled by flea collar angst," VIN News Service, (July 7, 2022), https://news.vin.com/default.aspx?pid=210&Id=11021199

the raw number of reported incidents will be higher for products that are more widely used. With 33 million collars sold in the U.S. alone, incident reports (most of which involve minor or moderate incidents) represent an extremely small proportion of the Seresto collars used. Moreover, those incidents need to be evaluated to determine whether the active ingredients may have caused the event based on the entire body of relevant scientific evidence—such as toxicity and safety studies—rather than viewed in isolation.

The Letter does not provide an analysis of incident data based on accepted pharmacovigilance principles. Instead, it asserts a number of unsupported criticisms of Seresto.

First, the Letter cites an EPA document released under the Freedom of Information Act, which the Letter characterizes as stating "'Seresto ranked #1 by a wide margin' in terms of total adverse incidents." Because this refers to *total* incident counts, *not* incidents when adjusted for total sales, this statement sheds little light on the safety profile of Seresto. As noted, the overall number of collars sold is an essential fact to consider in evaluating adverse incident reports.

The letter then cites the same EPA document for the premise that Seresto has a higher incidence reporting rate than other products. However, the cited EPA document itself acknowledges methodological shortcomings associated with this particular comparison, including "data inconsistencies," some sales data being approximated, and other limitations. In addition, the adverse events reported for Seresto are mostly mild or moderate reversible application site reactions. With respect to reports of death, the report rate for Seresto is similar to other marketed pet products in the Open FDA Animal & Veterinary Adverse Event database.[2]

Second, the Letter cites "data not previously available to the public" regarding a claimed causation analysis conducted by EPA and the Canadian PMRA relating to Seresto incident reports—but, that data is *still* unavailable to the public, and the Subcommittee has declined Elanco's request to provide the document containing that data. The Letter has pulled these percentages from an unreleased document, and so the basis for any such percentages is unknown. Without that information, these percentages cannot be meaningfully evaluated: we do not know which incidents were analyzed, how they were chosen, the criteria used to evaluate causation, or any other information about the methodology.

Through conversations with Subcommittee staff, Elanco has been able to obtain some information about what is in the underlying document, which the Subcommittee declined to provide to the public. Specifically, the Letter states that 45% of the 251 deaths EPA analyzed were determined to be possibly or probably related to the collar, but fails to include the important detail that only 2% of the 251 deaths were deemed probably caused by the collar, as Elanco understands the underlying document to reflect. The same is true of the Canadian PMRA's analysis, which Elanco understands found that 3% of the 251 deaths were probably caused by the collar. Thus, the vast majority of those percentages are "possible," not probable—a crucial distinction. Although we are not privy to how EPA or PMRA defined possible, "possible" generally means that there are other equally plausible or possible explanations for the incident, and is not a finding that the product likely caused the incident. Moreover, the "probable" events may include mechanical causes (for example, the collar getting

[2] Report rate is a proportional comparison, expressed as a percentage, representing the number of times a clinical sign was reported divided by the total number of cases, and thus can be calculated without access to the confidential sales data of other products.

caught on an object, an inherent risk for collars generally), rather than causes attributed to the active ingredients in the collar.

Third, the Letter cites ad hoc statements of particular EPA employees contained in documents released under FOIA. As EPA knows, there are rigorous, formal processes for evaluating data and reaching conclusions regarding safety. Those processes—which require a careful, science-based analysis of data—are the appropriate means to evaluate a product's safety.

Finally, the Letter does not discuss the significant benefits of Seresto, an essential element of any risk-benefit analysis. While all products have potential side effects, Seresto's benefits plainly outweigh any risks. Seresto provides broad coverage against fleas and ticks for 8 months in a convenient, affordable, and easy-to-use form. Fleas and ticks can carry serious and potentially fatal diseases, like Lyme disease and Rocky Mountain spotted fever and this public health concern is growing in severity.

* * *

Elanco is an animal health company, and is committed to improving the lives of animals. If it were in fact the case that Seresto posed an unreasonable risk to pets, we would remove it from the market. But that is not what the data show, and the Letter does not present a science-based analysis to the contrary. Based on the best available scientific evidence, Seresto is a safe and effective product that provides an important flea and tick control benefit. Elanco will continue to work cooperatively and transparently with EPA and FDA to ensure rigorous, science-based, data-driven, and non-politicized analysis of the safety profile of Seresto.

Respectfully submitted,

Kristin Bloink, DVM, MPH, DACVPM
Vice President, Global Regulatory
Affairs & Pharmacovigilance
Elanco US Inc.
2500 Innovation Way
Greenfield, IN 46140 USA
P: 712.898.9576
kristin.bloink@elancoah.com

cc: The Honorable Raja Krishnamoorthi, Chairman
Subcommittee on Economic and Consumer Policy

The Honorable Michael Cloud, Ranking Member
Subcommittee on Economic and Consumer Policy